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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/625,245 | 07/22/2003 | Shuichi Mizuno | 3831.08 | 9296 |
| 23308 PETERS VERI | 7590 05/18/200 NY L.I.P. | 7 | EXAM | INER |
| 425 SHERMAN AVENUE | | | NAFF, DAVID M | |
| SUITE 230 PALO ALTO, | CA 94306 | | ART UNIT | PAPER NUMBER |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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Advisory Action Before the Filing of an Appeal Brief

| Application No. | Applicant(s) | |
|-----------------|---------------|--|
| 10/625,245 | MIZUNO ET AL. | |
| Examiner | Art Unit | |
| | | |

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --THE REPLY FILED 26 April 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. 1. X The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods: The period for reply expires months from the mailing date of the final rejection. b) 🛮 The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f). Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b). **NOTICE OF APPEAL** 2. The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a). **AMENDMENTS** 3. 🔀 The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because (a) They raise new issues that would require further consideration and/or search (see NOTE below): (b) They raise the issue of new matter (see NOTE below); (c) They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal: and/or (d) They present additional claims without canceling a corresponding number of finally rejected claims. NOTE: See Continuation Sheet. (See 37 CFR 1.116 and 41.33(a)). 4. The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324). 5. Applicant's reply has overcome the following rejection(s): 6. Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s). 7. To purposes of appeal, the proposed amendment(s): a) will not be entered, or b) will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended. The status of the claim(s) is (or will be) as follows: Claim(s) allowed: None. Claim(s) objected to: Claim(s) rejected: 43-62. Claim(s) withdrawn from consideration: _____. AFFIDAVIT OR OTHER EVIDENCE 8. The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e). 9.

The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1). 10. The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached. REQUEST FOR RECONSIDERATION/OTHER 11.

The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet. 12. Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). 13. Other: ____. David M. Naff **Primary Examiner**

Art Unit: 1657

Continuation of 3. NOTE: (a) the claims raise new issues that would require further consideration and/or search. Claim 63 previously required a cartilage construct whereas claim 63 now requires a construct that is not required to be a cartilage construct. The claims now encompass a construct that contains a combination extracellular matrix and chondrocytes, and the percent of chondroctyes and the ratio in the last 3 lines of claim 63 encompass a construct containing mostly chondrocytes and very little extracellular matrix. New issues are further raised for consideration by step e) of claim 63 requiring applying hydrostatic pressure for "about one hour to about eight hours", subjecting to a resting period for "about eight hours to about twenty three hours", and the activation step being repeated for "about 1 day to about 60 days" since these ranges were not in the previous claims for applying hydrostatic pressure, resting and repeating activation. Additionally, the previous claims did not require repeating the activation step, and repeating the activation step further raises a new issue for consideration.

(b) the resting period of "about eight hours to about twenty three hours", and repeating the activation step for "about 1 day to about 60 days" raise the issue of new matter since these ranges are not found in the specification for resting and repeating activation. The range of "about 1 day to about 60 days" is disclosed as a resting period, and the range of "about eight hours to about twenty three hours" is nowhere found in the specification.

Continuation of 11. does NOT place the application in condition for allowance because: of reasons set forth in the previous office action and for reasons herein in response to arguments. The response urges that Smith et al nor the other references suggest the construct comprising rejuvenated chondrocytes able to produce new extracellular matrix produced by the process claimed. However, Smith et al isolate chondrocytes that are inherently mature (Example 1) since they are adult articular chondrocytes (col 16, line 65). These chondrocytes are inherently non-dividing and inactive. The present specification discloses no source of cartilage for isolating chondrocytes other than disclosed by Smith et al. Applying hydrostatic pressure at a frequency disclosed by Smith et al inherently rejuvenates the isolated chondrocytes as evidenced by Smith et al disclosing (col 11, lines 7-10) that the hydrostatic pressure increases metabolic activity and decreases expression of destructive enzymes of chondrocytes.